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|---|---|
| SIEW, JEFFREY | |
| ART UNIT | PAPER NUMBER |
| 1637 | 13 |

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/943,722 | Applicant(s) PAVLAKIS ET AL. | |
|---|---|---|---|
| | Examiner Jeffrey Siew | Art Unit 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *46-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *07 March 2003* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. This application contains claims 1,2,6-20,22,25-29 and 31-33 are drawn to an invention nonelected with traverse in Paper No.7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Pending claims to be examined are claims 46-49.

### *Double Patenting*

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 49 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No.6,414,132 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claim 49 is drawn to the **method of making** the synthetic gene.

Claims 1-12 of US 6,414,132 are drawn to a **method of making** a gene by substituting **less preferred codons with more preferred codon** in a inhibitory/instability sequence and introducing into a eukaryotic cell, culturing and expression (see in particular claim 1,6,9 & 12).

Claims 1-12 of US 6,414,132 are **not** drawn to a **mammalian expression**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells,** a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-12 of US 6,414,132 in order to produce the recombinant protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

3. Claim 49 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,174,666 in view of Coulombe.

Claim 49 is drawn to the **method of making** the synthetic gene. 1-9 of U.S. Patent No. 6,174,666

Claims 1-9 of U.S. Patent No. 6,174,666 are drawn to a **method of making** a gene by substituting **less preferred codons with more preferred codon** and introducing into a eukaryotic cell, culturing and expression (see in particular claim 1,6,9 & 12).

Claims 1-9 of U.S. Patent No. 6,174,666 are not drawn to a **mammalian expression**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells,** a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-9 of U.S. Patent No. 6,174,666 in order to produce the recombinant protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

4. Claims 46- 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-12 of U.S. Patent No. 6,291,664 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 3-12 & 33 of US 6,291,664 are drawn to **HIV env gene construct** with substituted less preferred codons with more preferred codon (e.g. see claim 3 SEQ ID NO:102 c substituted for wild type T at position 6686) and introducing into a vector and cell for expression.

Claims 3-12 & 33 of US 6,291,664 are **not** drawn to any **expression in mammalian cell** system.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells,** a form of **mammalian expression**. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 3-12 & 33 of US 6,291,664 in order to produce the recombinant env protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as claims 3-12 & 33of US 6,291,664 which are drawn to **HIV env gene**, represent a species of the genus claims 46-48 of the instant application which are drawn to **any** synthetic gene. The species would render the genus obvious.

5. Claims 46-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-6 of U.S. Patent No. 5,965,726 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 3-6 of US 5,965,726 are drawn to composition comprising a **HIV gag gene nucleic acid construct** with silent substituted **less preferred codons with more preferred codon** (e.g. see claim 3 SEQ ID NO:6 c substituted for wild type T at position 422 & Figure 4).

Claims 3-6 of US 5,965,726 are **not** drawn to any expression in **mammalian cell system**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells,** a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 3-6 of US 5,965,726 in order to produce the recombinant gag protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion). It would have been prima facie obvious to apply Coulomb et al's mammalian expression which were well known at the time the invention was made to the claimed method of substituting preferred codons in order to abundantly express mammalian proteins for analysis.

Moreover, as claims 3-6 of US 5,965,726 represent a species of HIV gag construct with silent substitution to produce a more preferred codon of the genus claims 46-49 of the instant claim which are drawn to any synthetic gene expressed in an eukaryotic cell with less preferred codon replaced by preferred codon. The species would render the genus obvious.

6. Claims 46-48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,972,596 in view of Coulombe et al (Gene vol. 46 pp 89-95 1986).

Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Claims 46-48 are drawn to any **synthetic gene** with less preferred codons replaced by preferred codon and **expression in mammalian cells**.

Claims 1-10 of U.S. Patent No. 5,972,596 are drawn to a **HIV gag nucleic acid construct** with silent substituted less **preferred codons with more preferred codon** (e.g. see claim 1 SEQ ID NO:6 c substituted for wild type T at position 422 & Figure 4).

Claims 1-10 of U.S. Patent No. 5,972,596 are not drawn to any expression in **mammalian cell system**.

Coulombe et al teach the construction of recombinant genes system, transfection in **murine cells,** a form of mammalian expression. In particular they express recombinant interferon gene (see whole doc. esp. page 90).

One of ordinary skill in the art would have applied Coulombe et al's teaching of murine expression of recombinant genes to the method claims 1-10 of U.S. Patent No. 5,972,596 in

order to produce the recombinant gag protein to study the role of different structural features of a gene in regulation of expression (see page 94 conclusion).

Moreover, as claims 1-10 of U.S. Patent No. 5,972,596 which are drawn to **HIV gag gene**, represent a species of the genus claims 46-48 of the instant application which are drawn to **any** synthetic gene. The species would render the genus obvious.

7. The response regarding the double patenting rejections filed 3/3/03 has been fully considered and deemed persuasive in part. The response states that the claims were originally subject to a restriction in parent 07/858747 now 6,174666. From this original restriction , the response contends that all the double patenting rejections made over the US patents from this lineage are therefore improper. Further examination of the file 07/858747 reveals that three groups were restricted. In group I claims 1-11 were drawn to method of reducing inhibitory/instability sequence of mRNA , classified in Class 435 subclass 6; Group II had claims 12-17 which were drawn to an expression method of producing said polypeptide encoded by mRNA classified in class 435 subclass 69.1; Group III had claims which were drawn to 18-33 were drawn to nucleic acid construct comprising said gene, kit, vector, transformed host which were classified across several class /subclasses including 536/27, 435/41,240.2 and 252.33. Indeed, US6,414,132 and US 6,174,666 are drawn to methods of making the gene which appears drawn to restricted group I. The double patenting rejections over claims 46-48 which are drawn to the product are withdrawn but still maintained over claim 49 which is drawn to the genus method of making. US 6,291,664 are drawn to specific HIV env gene construct. US 5,965,726 are also drawn to specific HIV gag gene construct. US5,972,596 are drawn to HIV gag construct.

These patented claims as the instant claims would fall within the same originally restricted group III which was drawn to nucleic acid constructs. The restriction is proper and maintained over US6,291,664, US5,965,726 and US5,972,596.

8. Regarding the above double patenting rejections, the response is also guided to MPEP 804 one way obviousness. If the application at issue is the later filed application or both are filed on the same day, only one-way determination of obviousness is needed in resolving the issue of double patenting (MPEP 800-23).

**THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY THE AMENDMENT**

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A review of the specification indicates that elements which are not particularly described including the inhibitory/instability region are essential to the

function of the claimed invention. The specification has disclosed a minimum number of species e.g. HIV gag and env gene. The location of the codon sequences of the inhibitory /instability region are empirically determined. These regions are widely varying across and within species. For example, these elements may be different from structural elements mediating the expression of the same protein in other organisms or even different organs within the same gene. Therefor the structure of this instability/inhibitory element which applicant considers as being essential to the function of the claim are not fully described to support the broad genus of the claims.

## SUMMARY

10. No claims allowed.

## CONCLUSION

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose telephone number is (703)-305-2982.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

JEFFREY SIEW
PRIMARY EXAMINER

April 18, 2003